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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,280	03/18/2004	Julia Golova	21416-95392	5570

23644 7590 03/21/2008

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EXAMINER	
LUNDGREN, JEFFREY S	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
03/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patent-ch@btlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/803,280	GOLOVA ET AL.	
	Examiner	Art Unit	
	JEFFREY LUNDGREN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 4-25* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 13-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 4-6 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 2 and 4-25 are pending in the instant application; claims 7-9 and 13-25 are withdrawn as being directed to a non-elected invention; and claims 2, 4-6 and 10-12 are the subject of the Office Action below.

Objection to the Abstract Under 37 C.F.R. § 1.72 - Withdrawn

The objection to the Abstract in the Office Action mailed on July 16, 2007, is overcome by Applicants' submission of an amended Abstract.

Objection of the Specification Under 37 C.F.R. §§ 1.821 - 1.825 - Withdrawn

The objection to the specification under 37 C.F.R. §§ 1.821 - 1.825 in the Office Action mailed on July 16, 2007, is withdrawn.

Claim Rejections - 35 USC § 102 - Withdrawn

The rejection of claims 1-6 under 35 U.S.C. § 102(b) as being anticipated by Vu *et al.*, *Bioconjugate Chem. 6*:599-607 (**1995**), in the Office Action mailed on July 16, 2007, is withdrawn in view of Applicants' cancellation of claims 1 and 3, and amendment to claim 2.

The rejection of claims 1-6 under 35 U.S.C. § 102(b) as being anticipated by Mullah *et al.*, U.S. Patent No. 5,736,626, issued on April 7, 1998, in the Office Action mailed on July 16, 2007, is withdrawn in view of Applicants' cancellation of claims 1 and 3, and amendment to claim 2.

Claim Rejections - 35 USC § 103 - Maintained

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of claims 2, 4-6 and 10-12, under 35 U.S.C. § 103(a) as being unpatentable over Mullah *et al.*, U.S. Patent No. 5,736,626, issued on April 7, 1998, in view of Vu *et al.*, *Bioconjugate Chem. 6*:599-607 (**1995**), is maintained.

Applicants generally allege that the combination of Mullah and Vu is not proper, and that the chemical differences between the protecting groups of Fmoc and TFA are so different that one of ordinary skill in the art would not possibly substitute one for another. Applicants make the assertion that:

> "Thus, in order to use the teachings of Mullah, it is inapposite to use a protecting group on the nitrogen that cannot be removed in the present of the DMT group. Such a modification of Mullah prevents the very synthetic process taught, namely the elaboration of the nucleotide prior to the incorporation of the label on the terminal hydroxyl group."

Applicants' Reply, page 9.

The Examiner disagrees. Both Fmoc and TFA protecting groups can be cleaved under mild basic conditions, whereas DMT is cleaved to yield a hydroxyl under acidic conditions. As evidenced by the teaching of Vu, Vu compares one compound for linking oligouncleotudes to CPG having a DMT/Fmoc group, and another compound having a DMT/TFA group. Mullah teaches the DMT/Fmoc scheme, and by reasonable interpretation of "or other like protecting groups," one clearly would find Applicants' arguments without merit.

Applicants continue to misconstrue the teachings in the art, and allege:

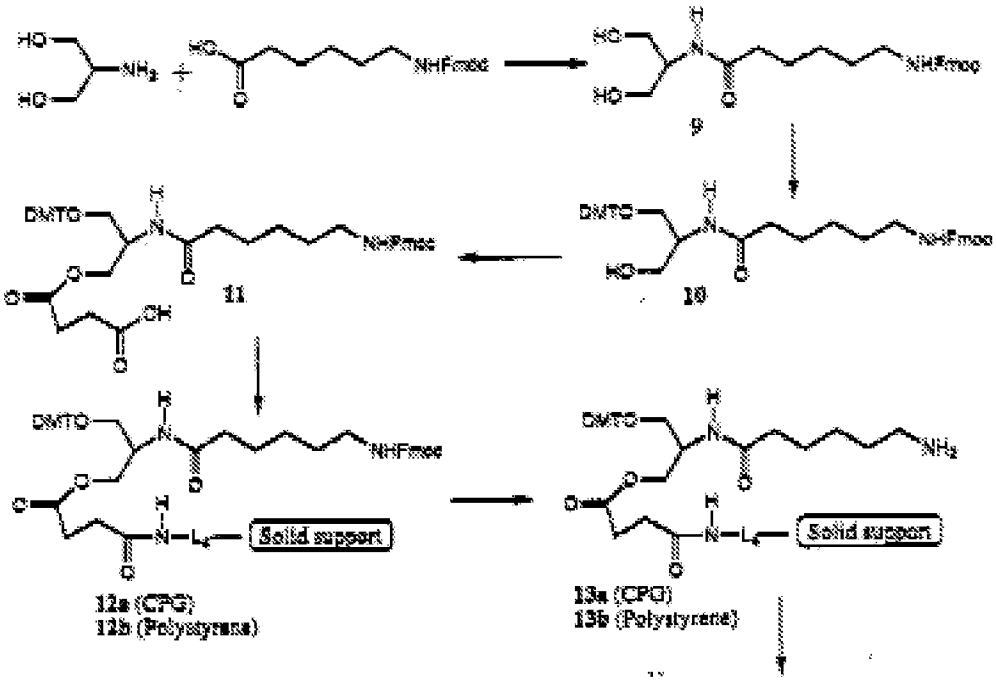
> "However, Vu teaches that for the purposes of delivering linkers capable of so- called 3'-amino modification after oligonucleotide elongation, the TFA group is unsuitable. They disclose that use of the TFA group in their synthetic sequence leads to the crude oligonucleotide mixture containing

> over 25% of materials derived from premature loss of the TFA group compared to no detectable levels of such products when one uses the phthaloyl protecting group that is the focus of their disclosure. A careful reading of the disclosure of Vu reveals that Vu, et al., teach away from the use of the TFA group for the purpose that Applicants have disclosed. Therefore, like Mullah above, Vu does not motivate the person of ordinary skill in the art to use the TFA protecting group in any context."

Applicants' Reply, page 10.

Again, the Examiner disagrees. As Vu makes quite clear, the synthesis of the DMT/Fmoc and the DMT/TFA oligo compounds are similar in terms of the percent yields (see page 607, col. 1, first full paragraph). Applicants comparison to the phthaloyl group is misplaced.

Mullah teaches compounds exemplified by the class of diglycolate synthesis supports particularly useful as support reagents for the direct synthesis of 3'-labeled polynucleotides. In particular, Mullah teaches the compounds as shown below taken from Figure 1:



Similar to the comparison of Vu, the compounds taught by Mullah meet the limitations of claims 1 and 2 (each of compounds 11, 12 and 13, as shown in Figure 1).

Mullah also teaches attachment of the linker compound to the solid support of controlled-pore glass (col. 6, lines 1-4), and therefore meets the limitations of claims 3-6.

Mullah also teaches that part of the chemistry used to attach the linker to the solid support involves a succinate, such as for attachment *via* the L4 part of the compound (col. 7, lines 35-40), and therefore meets the limitation for group X' in claim 10. Mullah also teaches compounds that have the value for m = 5, and n = 2, which is required by claims 10 and 11.

And although Mullah teaches nitrogen protecting groups such as Fmoc and others, Mullah does not explicitly teach the chemical group TFA as required by claim 10 and claim 11 (*i.e.*, $-C(O)CF_3$):

> "If a reactive amino group is desired subsequent to polynucleotide clearage [*sic*], R_1 and R_2 should not substantially interfere with the nitrogen reactivity. In this case, one of R_1 and R_2 is preferably lower alkyl, hydrogen, or a nitrogen protecting group, e.g., ***FMOC, tBOC, or other like nitrogen protecting groups***. Most preferably, one of R_1 and R_2 is hydrogen."

Mullah, col. 8, lines 21-27 (emphasis added).

Vu's compounds share a substantial chemical core with those of Mullah[1], and are useful for the same purpose (e.g., synthesizing oligonucleotides on a solid support, and having a protected amino group that can be deprotected at a later point, then labeled). In addition to teaching Fmoc as an amino protecting groups, Vu also teaches TFA protecting groups, such as those shown in compound 19 (see Figure 1, page 604).

Vu teaches compound compound 32[2] in Figure 1 on page 604; the claims are related to Vu's compound when Y is an optionally substituted second heteroatom (Vu's substituted nitrogen); when R is an oxygen protecting group (Vu's DMT); when X is an optionally

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[1] Compare Vu's compounds 19 in Figure 1 on page 604, with Mullah's compound 12 in Figure 1.

[2] Compound having the registry number: 170941-85-2; CN: *N*-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]glycyl-*N*-[2-[bis(4-methoxyphenyl)phenylmethoxy]-1-[(3-carboxy-1-oxopropoxy)methyl]ethyl]-Glycinamide

substituted heteroatom (Vu's amino-linked controlled pore glass – this disclosure also meets the limitations of claim 3-6).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Mullah and Vu teach chemical linking compounds for building oligonucleotides on solid supports with amino protecting groups that can be selectively removed and labeled. One of ordinary skill in the art would have been motivated to utilize other protecting groups with the core compound of Mullah, such as the TFA group as taught by Vu, because of the advantages rapid cleavage of TFA in basic environments (Vu, pages 606, cols. 1 and 2). Such an approach allows for subsequent cleavage and labeling with components of the linker molecule that are otherwise unstable in the presence of an acid, yet stable in the presence of a base (e.g., the chemistry involving the solid support or oligonucleotide). Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

The rejection is maintained.

Common Ownership of Claimed Invention Presumed

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. §§ 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Conclusions

No claim is allowable.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and

provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Schultz, can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JSL/

/Jon D. Epperson/
Primary Examiner, AU 1639